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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/850,363	05/07/2001	Michael Franciscus W. C. Martens	294-100	2538

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EXAMINER

COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 08/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/850,363

Applicant(s)

MARTENS ET AL.

Examiner

Gary W. Counts

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19,21-23,25,26 and 28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19,21-23,25,26 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims

The Request for Continued Examination filed June 28, 2004 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 19, 21-23, 25, 26 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is vague and indefinite because it is unclear if the dried form of the labeled monoclonal anti-insulin or anti-C peptide antibodies are actually part of the device or if they are placed within the device during assay procedures. Also, if the dried form of the antibodies is part of the device it is unclear how they are a part of the device. Are they immobilized to the device?

Claim 19 is vague and indefinite because it is unclear if the labeled monoclonal anti-insulin or anti-C peptide antibodies are the same or different antibodies as the capture monoclonal anti-insulin or anti-C peptide antibodies. Please clarify.

Claim 23 is vague and indefinite because it is unclear what arrangement allows the probe to be introduced in the Vena splenica and/or Vena porta. See also deficiencies found in claims 25 and 26.

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Claims 23, 25 and 26 are vague and indefinite because it is unclear how the sample further limits the device of Claim 19. It appears that claims 23, 25 and 26 are methods steps, which do not further limit the device.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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6. Claims 19, 22 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakanome et al (Immunoreactive proinsulin detected by enzyme-linked immunosorbent assay, Biomedical Research 18(5) 389-393, 1997) in view of Landa et al (US 4,626,684) and Milford et al (US 4,517,289).

Nakanome et al disclose a spectroscopic measurement device comprised of a microtiter plate and a microplate reader (page 390, column 2). Nakanome et al disclose that this microtiter plate contains wells (reservoirs) (page 389, column 2). Nakanome et al disclose that the well comprises monoclonal anti-C peptide antibodies and labeled anti-insulin antibody (see abstract). Nakanome et al disclose the addition of a washing solution to the well (page 389, column 2).

Nakanome et al differ from the instant invention in failing to specifically teach a photomultiplier detector. Nakanome et al also fails to teach the labeled monoclonal anti-insulin antibody present in dried form.

Landa et al disclose a photomultiplier detector for fluorescence immunoassay (abstract and column 6). Landa et al disclose that the use of this photomultiplier detector provides for rapid and sensitive analysis and is practical in the clinical environment (col 2, lines 40-68).

Milford et al disclose the use of lyophilized monoclonal antibodies along with any other necessary reagents (col 8, lines 65-68). This allows for the antibody to be in stable form (col 8, line 67).

It would have been obvious to one of ordinary skill in the art to substitute the photomultiplier detector such as taught by Landa et al for the microplate reader of

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Nakanome et al because Landa et al shows that the use of this photomultiplier detector provides for rapid and sensitive analysis and is practical in the clinical environment.

It also would have been obvious to one of ordinary skill in the art to incorporate the use of lyophilized antibodies as taught by Milford et al into the modified device of Nakanome et al because Milford et al shows that lyophilization of antibodies allows the antibodies to be in stable form. Further, it is well known in the art to lyophilize antibodies for preservation and storage purposes.

7. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakanome et al., Landa et al and Milford et al as applied to claims 19, 22 and 28 above, and further in view of Campbell et al (US 4,946,958).

See above for teachings of Nakanome et al., Landa et al and Milford et al.

Nakanome et al., Landa et al and Milford et al differ from the instant invention in failing to teach the label is a chemiluminescent label.

Campbell et al disclose a chemiluminescent label, which is conveniently linked to a monoclonal antibody or other protein and is used in an immunoassay for the quantitation of an antigen of interest (abstract). Campbell et al disclose that the use of this chemiluminescent label in assays provides a means of improving the sensitivity of measurement of proteins and polypeptides by one to two orders of magnitude (col 7, lines 27).

It would have been obvious to one of ordinary skill in the art to substitute the chemiluminescent label as taught by Campbell et al for the label of Nakanome et al because Campbell et al shows that the use of this chemiluminescent label in assays

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provides a means of improving the sensitivity of measurement of proteins and polypeptides by one to two orders of magnitude.

8. Claims 23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakanome et al., Landa et al and Milford et al as applied to claims 19, 22 and 28 above, and further in view of Schulz et al (Beziehungen zwischen den portalen and peripher-venosen Insulin-, proinsulin, Band 68 Heft 3, pp. 309-318 (1976)).

See above for teachings of Nakanome et al., Landa et al and Milford et al.

Nakanome et al., Landa et al and Milford et al differ from the instant invention in failing to teach obtaining the sample by a probe arranged to be introduced in the Vena porta.

Schulz et al disclose obtaining a sample by insertion of a catheter (probe) in the portal vein (page 309). Obtaining a sample in this manner provides for a sample that can be used as a diagnostic tool of pancreatic hormone secretion in man and also provides significantly enhanced portal IRI concentrations and increased PLM (proinsulin-like material).

It would have been obvious to one of ordinary skill in the art to obtain a sample as taught by Schulz et al for the modified device of Nakanome et al because Schulz et al shows that obtaining a sample in this manner provides for a sample that can be used as a diagnostic tool of pancreatic hormone secretion in man and also provides significantly enhanced portal IRI concentrations and increased PLM (proinsulin-like material).

9. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakanome et al., Landa et al., Milford et al and Campbell et al as applied to claims 19,

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21, 22 and 28 above, and further in view of Schulz et al (Beziehungen zwischen den portalen and peripher-venosen Insulin-, proinsulin, Band 68 Heft 3, pp. 309-318 (1976).

See above for teachings of Nakanome et al., Landa et al., Milford et al. and Campbell et al.

Nakanome et al., Landa et al., Milford et al and Campbell et al differ from the instant invention in failing to teach obtaining the sample by a probe arranged to be introduced in the Vena porta.

Schulz et al disclose obtaining a sample by insertion of a catheter (probe) in the portal vein (page 309). Obtaining a sample in this manner provides for a sample that can be used as a diagnostic tool of pancreatic hormone secretion in man and also provides significantly enhanced portal IRI concentrations and increased PLM (proinsulin –like material).

It would have been obvious to one of ordinary skill in the art to obtain a sample as taught by Schulz et al for the modified device of Nakanome et al because Schulz et al shows that obtaining a sample in this manner provides for a sample that can be used as a diagnostic tool of pancreatic hormone secretion in man and also provides significantly enhanced portal IRI concentrations and increased PLM (proinsulin –like material).

Response to Arguments

10. Applicant's arguments filed June 28 2004 have been fully considered but they are not persuasive.

Applicant argues that Nakanome et al disclose an assay for measuring pro-insulin and that the Nakanome et al state that that their assay is specific for proinsulin, and

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failed to detect both insulin and C-Peptide. This is not found persuasive because as stated in the previous office action and the advisory action the recitation "a real-time insulin test system" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Therefore, the claim merely requires a reservoir comprising monoclonal anti-C peptide antibodies coated to the reservoir (limitations taught by Nakanome et al., See previous office action for teachings of Nakanome et al). Applicant further argues that Nakanome requires a lengthy incubation period. This is not found persuasive because of reasons stated above concerning the recitation "real time" in the preamble of the claim. Further, although the applicant argues that Nakanome does not teach a "real time" insulin test system, the instant claims do not make clear nor are they limited to a "real time" test system. For example, there are no structural or functional limitations positively recited in the claims to support a "real time" test system.

Also with respect to the argument that Nakanome et al disclose an assay for measuring pro-insulin and that the Nakanome et al state that that their assay is specific for proinsulin, and failed to detect both insulin and C-Peptide. This argument is directed

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to method of use, while the claims are directed to a test system, therefore the argument is not on point.

Applicant also argues that the claimed invention is an assay kit for detecting insulin and therefore, the assay of Nakanome et al. differs from the claimed invention. This is not found persuasive because Applicant is arguing away from the claims. Nowhere in the claims is there a recitation stating an assay kit. The preamble of the claim recites "A real-time insulin test system" which reads as a device and not a kit.

Applicant argues that Landa et al. merely disclose a fluorescence analyzer and that nowhere in Landa et al. is there any disclosure or suggestion of a real-time assay to measure insulin levels using monoclonal anti-insulin or anti-C peptide antibodies useful as a tracer in the reservoir. This is not found persuasive because Examiner has not relied upon Landa et al for teachings these limitations. As discussed above, Nakanome teaches these limitations. Examiner has relied upon Landa et al for teaching the advantages of photomultiplier detector for fluorescence immunoassay. Furthermore, Nakanome et al specifically teaches a spectroscopic measurement device. Therefore, It would have been obvious to one of ordinary skill in the art to substitute the photmultiplier detector such as taught by Landa et al for the fluorescence analyzer of Nakanome et al because Landa et al shows that the use of this photomultiplier detector provides for rapid and sensitive analysis and is practical in the clinical environment.

Applicant argues that Milford et al discloses that their kit can contain HLA antibodies in lypholized form, as well as other reagents and accessories, such as a reaction vessel and thus Milford teach the antibody in lyophilized form and the reaction

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vessel are two separate components of the kit. This is not found persuasive Examiner has not relied upon Milford for teaching the labeled antibody in the reservoir. Examiner has relied upon Nakanome et al for teaching the antibody in the reservoir. Further, it is unclear if the labeled antibody is part of the reservoir or not (see 112 2nd rejection of claim 19 above). Examiner has relied upon Milford et al for the teaching that it is known in the art to lyophilize antibodies and that this lyophilization provides the advantage of stabilizing antibodies. Therefore, it is the Examiner's position that the combination of Nakanome et al., Landa et al. and Milford et al is proper and reads on the instantly rejected claims.

Applicant's argues that the combination of Nakanome et al. and Landa et al., in view of Campbell does not teach all of the claim limitations and that Applicants have demonstrated the importance of using monoclonal anti-insulin or anti-C peptide antibodies useful as a tracer in the reservoir in dried form, in the test system. This is not found persuasive because Examiner has not relied upon Nakanome et al., Landa et al., and Campbell et al for teaching the antibodies in dried form but rather has relied upon Milford et al for teaching the advantages of antibodies in dried form (see above for teachings of Milford).

Applicant's argues that Nakanome et al. and Landa et al., Milford et al., in view of Shultz does fails to teach monoclonal anti-insulin or anti-C peptide antibodies useful as a tracer in the reservoir in dried form. This is not found persuasive because as stated above Nakanome et al teaches the antibody in the reservoir. Further, it is unclear if the labeled antibody is part of the reservoir or not (see 112 2nd rejection of

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claim 19 above). Examiner has relied upon Milford et al for the teaching that it is known in the art to lyophilize antibodies and that this lyophilization provides the advantage of stabilizing antibodies. Also, it is unclear how the sample further limits the device (see 112 2nd rejection above). Therefore, it is the Examiner's position that the combination of Nakanome et al., Landa et al., Milford et al and Shultz et al is proper and reads on the instantly rejected claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

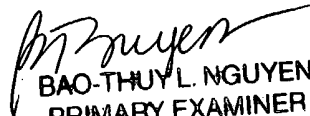

Gary W. Counts
Examiner

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August 2, 2004


BAO-THUY L. NGUYEN
PRIMARY EXAMINER
8/4/04